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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#2F4107. Difenoconazole (**Dividend**) in/on Wheat, Barley, and Animal RACs. Review of Residue Data and Analytical Methodology. MRID#s 428065-04 & -05; 428180-01, -02, -03, -04, -05 & -06; 422451-41; 422451-01; & 431203-01. Barcodes D194842, D199810, D199580 & D195868. Case 283543. CBTS#s 12495, 13281, 13249 & 12682.

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3/29/94

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And

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CIBA-GEIGY Corporation proposes tolerances for residues of the fungicide difenoconazole (1-{2-[4-(4-chlorophenoxy)-2-chlorophenyl]-4-methyl-1,3-dioxolan-2-yl-methyl}-1*H*-1,2,4-triazole) on wheat, barley and animal RACs and as the result of seed treatment. The proposed tolerances are as follows:

Wheat Grain	--	0.1 ppm	Barley Grain	--	0.1 ppm
Wheat Forage	--	0.1 ppm	Barley Forage	--	0.1 ppm
Wheat Straw	--	0.1 ppm	Barley Straw	--	0.1 ppm
Milk	--	0.01 ppm	Eggs	--	0.05 ppm
Fat*	--	0.05 ppm	Poultry Fat	--	0.05 ppm
Meat*	--	0.05 ppm	Poultry Meat	--	0.05 ppm
Meat By-Products*	--	0.05 ppm	Poultry Meat By-Products	--	0.05 ppm

*of cattle, goats, horses, hogs and sheep

The following tolerances were also proposed in conjunction with PP#2E4051 (foreign registration):

Wheat Grain	--	0.1 ppm
Barley Grain	--	0.1 ppm
Rye Grain	--	0.1 ppm

In review of PP#2E4051, CBTS identified the deficiencies in the submitted data which must be addressed by the registrant in order for us to be able to recommend in favor of tolerances for a domestic registration. All remaining deficiencies specific to the import tolerances (PP#2E4051) for difenoconazole must also be resolved before CBTS could recommend in favor of this domestic registration.

In the Detailed Considerations section of this Memo, the outstanding deficiencies which apply to the domestic registration, listed as presented in the Memo of R. Lascola (10/26/92), are followed by the petitioner's response and our conclusions.

RECOMMENDATIONS

CBTS recommends against the proposed tolerances for difenoconazole on wheat, barley and animal RACs for reasons detailed in conclusions 1, 2b, 3, 4b, 5b, 7b, 8b and 9b.

CONCLUSIONS

1. The following deficiencies in the Product Chemistry remain outstanding: a) while the petitioner has come up with reasonable scenarios for the formation of observed impurities, the possibility of other impurities that may result from additional side reactions should be discussed. b) In order to fulfill the requirements of Guideline 63-13, the registrant should submit further information on the procedure and results of experiments used to determine the stability of the TGAI to metals and sunlight and report on the stability of the TGAI to metal ions. c) Submission of a CSF for Dividend 3SF (in conjunction with PP#2E4051 - Memo, G. Kramer 1/10/94)

2a. Difenoconazole can be applied to seeds of wheat and spring barley at a maximum rate of 10.9 g. ai/100 lbs. seed.

2b. The directions for use are adequate except that no crop rotation restrictions are specified. Until completion of the crop rotation studies (see below), the label should restrict crop rotation to barley and wheat by adding a statement such as "do not plant back any crops other than barley and wheat within one year to

fields in which treated seeds were planted." **A revised Section B is required.**

3. The registrant has requested a waiver for rotational crop studies due to the anticipation of low residues in such crops as a result of the low application rate (equivalent to 0.34 oz. ai/A) and the short soil halflife. Based on the results of plant metabolism studies, it appears to be likely that a rotational crop planted 30 days after treatment (simulating crop failure) would contain significant (>0.01 ppm) residues. Another reason for these confined studies is to determine whether rotational crops are bioaccumulating soil metabolites of regulatory concern. This information can not be determined without actually performing the study. The registrant should provide the rotational crop studies for our review.

4a. The nature of the residue in barley and wheat grain is **not** considered to be understood. The major residues are triazole alanine and triazole acetic acid.

4b. The registrant should provide: **1)** chromatographic evidence of storage stability of the labelled grain, straw and forage samples; **2)** further characterize the nature of the residue in the triazole-labelled seed-treated grain samples by performing the same procedures on the seed-treated grain samples as were performed on the foliar-treated samples and also further characterizing/identifying any fraction which contains >10% of the TRR or >0.05 ppm (i.e., Zones A, B and C from TLC separation). If there is insufficient radioactivity in these Zones for adequate identification/characterization, then the foliar-treated grain samples should be further characterized. The registrant must convince us that there is no single unidentified compound which exceeds these trigger values in the seed-treated grain sample; and **3)** characterize the nature of the residue in both the phenyl- and triazole-labelled whole plants harvested 40 days after planting.

4c. Pending the demonstration of storage stability, CBTS considers the nature of the residue in wheat straw (stalks) to be understood.

5a. The **nature** of the residue in animals is **not** considered to be adequately understood.

5b. The registrant has not provided the information we previously requested (Memo, R. Lascola 10/26/92). In order for CBTS to be able to determine the nature of the residue in animals, the petitioner must address the following concerns: **a)** The petitioner has failed to take all reasonable steps to identify or release aqueous phase and conjugated metabolites which comprise up to half of the observed activity in several tissues. The petitioner has not noted the effects of acidic or basic hydrolysis on these metabolites, nor has mass spectrometry been used to identify the metabolites. **b)** While the metabolite CGA-205375 appears to be the

major organic-soluble metabolite, inconsistencies between the triazole- and phenyl-labeled experiments bring the measured residue levels of this compound into question. Specifically, bridge-intact metabolites should appear in approximately the same proportion in the two studies, and they do not. CBTS asks the petitioner to resolve these inconsistencies. **c)** The petitioner should also explain the large radioactivity recoveries (>>120%) reported for several samples. If the petitioner has stored extra samples from these studies under frozen conditions, reanalysis of the tissues may be attempted, taking care to address the concerns listed above. In that event, the petitioner should also supply information detailing the stability of the chemical and metabolites under the storage conditions. Otherwise, the petitioner will have to reconduct these studies.

6. Existing analytical enforcement methodology is adequate to support the requested difenoconazole tolerances on wheat and barley RACs (Memo, G. Kramer. 1/10/94). The method is described in MRID# 428065-04 and has undergone successful Petition Method Validation (PMV) for the parent compound, difenoconazole.

7a. The registrant has submitted a proposed analytical enforcement method and Independent Lab Validation (ILV) for animal RACs. Acceptable recoveries were obtained for each RAC at the level of the proposed tolerances.

7b. We have forwarded the analytical method and ILV to the ACL, Beltsville for the PMV. CBTS will withhold its conclusion on the adequacy of method AG-544 as an analytical enforcement method for difenoconazole residues in meat, milk and eggs pending the outcome of the PMV.

8a. The registrant has shown storage stability in lettuce, soybeans and wheat forage for a period of 1 yr.

8b. Further studies are needed to demonstrate storage stability in the RACs wheat (or barley) grain and straw.

9a. The registrant has referenced previously submitted magnitude of the residue studies. Only 4 acceptable winter trials in states representing 38% of the U.S. winter wheat acreage (in 1991, *Agricultural Statistics 1992*) and no U.S. barley field trials were performed.

9b. CBTS concludes that this data is not adequate to support this request for domestic tolerances on wheat and barley RACs. The number of field trials and geographic representation is insufficient for winter wheat. In addition, the registrant failed to generate data for wheat hay, which may be reinstated as a RAC in Table II. Wheat hay was in the original Table II, but then deleted as announced in the FIFRA '88 Phase 3 Technical Guidance Package. It may be reinstated in the forthcoming revision of Table II.

Also, data from barley field trials in the U.S. should be submitted to support tolerances on this crop. The registrant is requested to perform at least 4 barley field trials (in ND, MT, MN plus one other state such as ID, SD or WA) and at least 8 additional wheat field trials (in KS, OK, CO, NE and WA plus three other state such as MO, SD, MT, OH, IL or IN). Residue data for grain, straw and forage should be obtained in these trials. **Data for and a revised Section F with proposed difenoconazole tolerances on wheat and barley hay may also be required in the future.**

10a. Based on the low potential for transfer of residues to animal tissues, the registrant has proposed to allow the animal metabolism studies to also serve as feeding studies.

10b For now, CBTS is willing to accept this proposal. If higher levels of difenoconazole residues than previously observed are found in the new wheat or barley field trials or if the Metabolism Committee determines that metabolites other than *difenoconazole per se* to be of regulatory concern, then CBTS may require the registrant to perform conventional feeding studies.

11. There are no Codex, Canadian, or Mexican tolerances for difenoconazole on wheat, barley, or rye grains. Therefore, no compatibility problems are anticipated with this tolerance request.

Note to PM: When this tolerance is established, it should be as [(2S,4R)/(2R,4S)]/[(2R,4R)/(2S,4S)]1-{2-[4-(4-chlorophenoxy)-2-chlorophenyl]-4-methyl-1,3-dioxolan-2-yl-methyl}-1*H*-1,2,4-triazole.

DETAILED CONSIDERATIONS

PRODUCT CHEMISTRY

Deficiency - Conclusion 1a (from Memo, R. Lascola 10/26/92)

For future domestic registrations, the fungicidally active enantiomers should be identified.

Petitioner's Response: All enantiomers have approximately equal pesticidal activity (MRID# 428065-01c).

CBTS' Conclusion: The requested information has been provided. This deficiency is now resolved.

Deficiency - Conclusion 1d (from Memo, R. Lascola 10/26/92)

CBTS notes that while the petitioner has come up with reasonable scenarios for the formation of observed impurities, the possibility of other impurities that may result from additional side reactions will need discussion for any future tolerance petition.

Petitioner's Response: "There has been no reaction among any of the ingredients in the formulation as evidenced by the absence of any extraneous peaks as detected by capillary GC analysis in either heated samples or room temperature samples." (MRID# 428065-01c)

CBTS' Conclusion: The registrant has previously accounted for [redacted] impurities listed in the CSF. We asked for a theoretical discussion of the formation of impurities which could possibly be formed during the manufacturing process but were not actually observed at a level of >0.1 ppm. The registrant has merely stated that they have not detected the presence of such impurities. The requested information has not been provided. **This deficiency remains outstanding.** The registrant should provide a theoretical discussion of possible impurities under conditions of the manufacturing process.

Deficiency - Conclusion 1f (from Memo, R. Lascola 10/26/92)

The petitioner has not discussed the justification for the certified limits. The petitioner should submit an explanation of how they arrived at their certified limits.

Petitioner's Response: The limits for the TGAI were determined based on the five batch analysis. The proposed limits for all impurities were determined based on the quantity of this impurity present in the beginning material and variations which can occur within the parameters of the manufacturing process (MRID# 428065-02c).

CBTS' Conclusion: The requested information has been provided. This deficiency is now resolved.

Deficiency - Conclusion 1g (from Memo, R. Lascola 10/26/92)

The method for determination of the cis/trans ratio of the active ingredient involves use of a "Spectra-Physics SP 8773" detector. The petitioner should indicate what type of detector it is.

Petitioner's Response: The SP-8773 detector is a variable wavelength UV-Vis detector (MRID# 428065-02c).

CBTS' Conclusion: The requested information has been provided. This deficiency is now resolved.

Deficiency - Conclusion 1h (from Memo, R. Lascola 10/26/92)

For both Methods AW-128/2 and AK-128/2, the petitioner suggests that the methods were validated at an outside laboratory. The petitioner should submit the reports from the outside laboratory. Those reports should include at least the name and location of the laboratory, a description of the procedure, a record of any communication between that laboratory and the petitioner concerning the execution of the method, sample chromatograms, and results.

Petitioner's Response: The validations were not performed at an outside laboratory. All of the validation data were given in the validation reports included in the original submission (MRID# 428065-02c).

CBTS' Conclusion: The requested information has been provided. This deficiency is now resolved.

Deficiency - Conclusion 1j (from Memo, R. Lascola 10/26/92)

The information submitted for Section 63-13, stability of the TGAI, is incomplete. The petitioner must also submit data describing the stability of difenoconazole in the presence of metal and metal ions, and also in sunlight, for any future tolerance request requiring registration of this product.

Petitioner's Response: MRID# 428065-03. **Metals:** The TGAI was evaluated for stability when stored with four different metals: carbon steel, stainless steel, aluminum and tinplate. The samples were placed at 38 °C and room temperature and evaluated over 26 weeks. No decomposition of the TGAI was observed. **Sunlight:** The TGAI was evaluated for stability when exposed to a xenon arc lamp. The sample was placed in an open beaker for 24 hrs of continuous exposure to the lamp. No decomposition of the TGAI was observed.

CBTS' Conclusion: The methods used in these tests were not described in detail. The registrant should provide additional information on the procedures used; i.e., the physical form of the metals (e.g. containers, filings etc.), the physical form of the TGAI (solid or solution) and the analytical method used to determine the percent decomposition. Also, the results should be described in greater detail; i.e., report on whether there was any evidence of a chemical reaction (e.g. color change) and report the numerical results for the sunlight stability experiment. If a solution of the TGAI was used to evaluate the stability to metals or sunlight, then the test should be repeated using the solid material. The registrant has also not provided any information on the stability of the TGAI to metal ions. In order to fulfill the requirements of Guideline 63-13, the registrant should submit further information on the procedure and results of experiments used to determine the stability of the TGAI to metals and sunlight and report on the stability of the TGAI to metal ions. **This deficiency remains outstanding.**

Table 1- PRODUCT CHEMISTRY DATA SUMMARY
Chemical No. 128847
Product: Difenoconazole TGAI

Guideline Number	Requirement	Are Data Requirements Fulfilled? [a]	MRID Number
61-1	Product Identity and Disclosure of Ingredients	Y	420900-01 & -02 428065-01
61-2	Beginning Materials and Manufacturing Process	Y	420900-01 & -02 428065-01
61-3	Discussion of Formation of Impurities	N[b]	420900-01 & -02 428065-01, 422451-01
62-1	Preliminary Analysis	Y	420900-01 & -02 428065-02
62-2	Certification of Ingredient Limits	Y	420900-01 & -02 428065-02
62-3	Analytical Methods to Verify the Certified Limits	Y	420900-01 & -02 428065-02
63-2	Color	Y	420900-03
63-3	Physical State	Y	420900-03
63-4	Odor	Y	420900-03
63-5	Melting Point	Y	420900-03
63-6	Boiling Point	N/A	
63-7	Density, Bulk Density or Specific Gravity	Y	420900-03
63-8	Solubility	Y	420900-03
63-9	Vapor Pressure	Y	420900-03
63-10	Dissociation Constant	Y	420900-03
63-11	Octanol/Water Partition Coefficient	Y	420900-03
63-12	pH	Y	420900-03
63-13	Stability	N[c]	428065-03
63-14	Oxidizing or Reducing Action	N/A [d]	422451-01
63-15	Flammability	N/A [d]	422451-01
63-16	Explodability	N/A [d]	422451-01
63-17	Storage Stability	N/A [d]	422451-01
63-18	Viscosity	N/A [d]	422451-01
63-19	Miscibility	N/A [d]	422451-01
63-20	Corrosion Characteristics	N/A [d]	422451-01

[a] Y = Yes; N = No; N/A = Not Applicable.

[b] Discussion of theoretical impurities required.

[c] Stability to metal ions not reported plus further information on the procedure and results of experiments used to determine the stability of the TGAI to metals and sunlight is required.

[d] Data are not required for the TGAI.

Proposed Use

Dividend is a flowable concentrate of difenoconazole containing 3 lbs. ai/gal. Dividend is applied as a water-based slurry by mixing by with up to 16 oz. water per 100 lbs. seed. The maximum use rate is 1 fluid oz./100 lbs. seed (10.9 grams or 0.38 oz./100 lbs. seed). These instructions differ from the foreign registration for Dividend 150FS (see Memo, R. Lascola 10/26/92) in that the use on barley is restricted to spring barley, the maximum use rate is lower (27.2 g. ai/100 lbs. seed for Dividend 150FS) and there is no use specified for rye.

The label contains the following restrictions: a) do not use treated seed for feed, food or oil; b) green forage may not be grazed until 55 days after planting; c) do not apply to winter barley; d) for use only by commercial seed treaters.

The directions for use are adequate except that no crop rotation restrictions are specified. Until completion of the crop rotation studies (see below), the label should restrict crop rotation to barley and wheat by adding a statement such as "do not plant back any crops other than barley and wheat within one year to fields in which treated seeds were planted." **A revised Section B is required.**

Rotational Crops

The registrant has submitted a waiver for rotational crop studies (MRID# 422451-41). The rationale behind this request is based on the low application rate and short soil halflife of difenoconazole. If seed is treated at the maximum use rate (10.9 g/100 lbs. seed) and planted at the maximum seeding rate (90 lbs./A), the application rate is equivalent to 0.34 oz. ai/A. This rate equates to 0.022 ppm difenoconazole in the top 3 inches of soil. The soil halflife of 0.1 ppm difenoconazole is 63 days. However, the petitioner also cites plant metabolism studies in which residues of up to 0.18 ppm were found in the primary crop at harvest. It thus appears to be likely that a rotational crop planted 30 days after treatment (simulating crop failure) would contain significant (>0.01 ppm) residues. Another reason for these confined studies is to determine whether rotational crops are bioaccumulating soil metabolites of regulatory concern. This information can not be determined without actually performing the study. CBTS has previously denied a waiver request for rotational crop studies on the seed fungicide oxadixyl for similar reasons (Memo, G. Herndon 2/5/93). In the case of difenoconazole, CBTS recommends **against** granting the waiver request for rotational crop studies. Until completion and review of acceptable rotational crop studies, the label directions for use of difenoconazole should specify that crop rotation is restricted to barley and wheat by adding a statement such as "do not plant back any crops other than barley and wheat within one year to fields in which treated seeds were planted."

NATURE OF THE RESIDUE-WHEAT

Deficiency - Conclusion 2 (from Memo, R. Lascola 10/26/92)

The petitioner has NOT adequately determined the nature of the residue in wheat. For future domestic tolerance requests, these following major deficiencies associated with the submitted studies will need to be resolved: 1) The petitioner has been able to characterize and/or quantitate only a small fraction of the activity in any sample, but particularly for those samples originating from seed-treated plants. In many cases, such as grain and stalk samples in MRID# 420900-33, no characterization was achieved. In other examples, such as the grain and stalk samples in MRID# 420900-34, where the activity was (partially) characterized, only rarely was the petitioner able to quantitate the activity. In addition, large portions of the activity (15% - >25%) could not be accounted for after the extraction procedures. The petitioner must be able to characterize and quantitate the residues in wheat grain and stalks before CBTS and TOX can assess the need to regulate metabolites of CGA-169374. 2) The petitioner did not carry out all the extraction or analysis procedures that would be expected. For example, several times no attempt was made to analyze the organic layer of grain or stalk sample separations. Also, the petitioner did not use enzymes besides β-glucosidase to release bound residues. Since significant fractions (up to 65%) of the activity were "bound", the petitioner must demonstrate that all reasonable efforts have been made to release and identify those residues.

Petitioner's Response: MRID# 428180-01. CBTS previously reviewed three wheat metabolism studies- a field study with seed application (MRID# 420900-34), a greenhouse study with seed application (MRID# 420900-33) and a greenhouse study with foliar application (MRID# 420900-32). In each study, difenoconazole was applied in phenyl- and triazole-labelled forms. Significant residues in mature plants as a result of seed treatment were found only in studies in which the triazole-labelled compound was used. In response to our previous review, the registrant has performed further metabolite identification on the samples from these studies. These samples were stored frozen for ≈2 years between the conclusion of the previous work and the initiation of the present study. The registrant reports that storage stability was demonstrated by comparison of the extractability and chromatographic characteristics in the present study with the previous findings. Table 2 shows that the extractability of the samples is generally unchanged during storage. The only major difference observed was in the TRR of one grain sample (greenhouse, seed-treated) which apparently increased during storage. This result was attributed to desiccation and/or incomplete homogenization of the sample. No chromatographic evidence of storage stability was provided.

Table 2- Results of fractionation of triazole-labelled samples before and after 2 years of storage.

Site	Treatment	RAC	TRR (ppm)	% TRR			
				Organic	Aqueous	Bound	Total
Before Storage							
Field	Seed	Straw	0.059	9.42	87.12	16.08	112.62
Green-House	Seed	Straw	0.069	16.80	71.60	18.30	106.70
		Grain	0.183	0.00	80.40	25.30	105.70
	Foliar	Straw	53.80	50.10	27.40	13.20	90.70
		Grain	1.400	0.00	69.50	22.70	92.30
After Storage							
Field	Seed	Straw	0.061	8.1	86.7	13.7	108.5
Green-House	Seed	Straw	0.081	12.9	57.5	33.6	104.0
		Grain	0.583	0.0	79.0	36.0	115.0
	Foliar	Straw	53.80	54.4	23.0	16.1	93.5
		Grain	1.192	0.0	90.0	30.0	120.0

Grain: Aqueous-soluble grain residues were applied to a Sephadex A-25 column, resulting in two peaks. The major peak (peak 1, 40-68% of the TRR) was acetylated and separated into four zones by preparative TLC. Zone C was identified as free triazole (CGA-71019, fig. 1) by 2D-TLC. In the grain from the seed-treated samples, 13.0% of the TRR was identified as triazole. No further analysis of this sample was reported. The work on the foliar-treated grain samples was extended by analysis of peak 2 from the sephadex column. After butylation, the majority of this peak coeluted with triazole acetic acid (CGA-142856) on 2D-TLC. This identification was confirmed by GC/MS. The postextraction solids were treated with cellulase, releasing 76% of the bound residues. After acetylation, the released residues were separated into four separate zones by preparative TLC. Zone C (triazole) contained 11.7% of the TRR. Overall, 49.3% of the TRR was identified as triazole and 16% as triazole acetic acid for a total of 65.3% of the TRR identified (Table 3). The metabolism of difenoconazole in foliar- and seed-treated wheat grain appears to be very similar.

Table 3- Distribution of TRR in foliar-treated triazole-labelled wheat grain. "Bound" residues were analyzed after being released by cellulase treatment.

Component	Soluble		Bound		Total	
	ppm	% TRR	ppm	% TRR	ppm	% TRR
Triazole	0.448	37.6	0.139	11.7	0.587	49.3
Triazole Acetic Acid	0.191	16.0	ND	-	0.191	16.0
Zone A	0.057	4.8	0.012	1.0	0.069	5.8
Zone B	0.111	9.3	0.050	4.2	0.161	13.5
Zone D	0.087	7.3	0.136	11.4	0.223	18.7
Unextractable	-	-	0.113	9.5	0.113	9.5

Straw (Stalks): The foliar-treated, greenhouse-grown straw samples were initially extracted in methanol/water. The extractable residues (77.9% of the TRR) were partitioned into organic (chloroform)-soluble (54.4% of the TRR) and aqueous-soluble (23.0% of the TRR) fractions. The organic soluble fraction was initially analyzed by 2D-TLC. Of the six spots, four appeared to coelute with standards- triazole (3.37% of the TRR), CGA-205375 (2.2% of the TRR), CGA-205374 (0.49% of the TRR) and difenoconazole *per se* (43.3% of the TRR). For further analysis, the organic fraction was separated into five zones on preparative TLC. Each zone was analyzed by 2D-TLC. Components in two zones were found to coelute with standards- CGA-205375 and difenoconazole *per se*. The identification of these compounds was confirmed by HPLC and MS. The aqueous-soluble fraction (23% of the TRR) was cleaned-up using a Sephadex A-25 and C-18 columns and characterized by 2D-TLC. Of the 11 spots, two coeluted with standards- CGA-205375 (0.3% of the TRR) and difenoconazole (1.2% of the TRR). Another portion of the aqueous-soluble fraction was treated with cellulase and then extracted with ethyl acetate. 2D-TLC was used to separate the ethyl acetate fraction (19.5% of the TRR) into 10 components, three of which corresponded to standards- CGA-205375 (13.4% of the TRR), CGA-205374 (0.5% of the TRR) and difenoconazole *per se* (0.8% of the TRR). The identity of CGA-205375 was confirmed by HPLC and MS. The bound residues (16.1% of the TRR) were treated with protease and partitioned with ethyl acetate. The aqueous phase contained 8.0% of the TRR; the organic phase, 2.1%; and 5.7% remained unextractable. 2D-TLC analysis of the organic phase revealed the presence of 11 components, four of which coeluted with standards- triazole (0.06% of the TRR), CGA-205375 (0.39% of the TRR), CGA-205374 (0.02% of the TRR) and difenoconazole *per se* (0.13% of the TRR). The aqueous fraction was butylated, cleaned-up and separated by preparative TLC. 2D-TLC analysis indicated the presence of triazole alanine (1.4% of the TRR), triazole acetic acid (1.1% of the TRR), triazole (1.7% of the TRR), CGA-205375 (1.0% of the TRR) and CGA-205374

(0.6% of the TRR). The results of the residue identification are summarized in Table 4. A total of 72% of the TRR was identified in the foliar-treated straw sample.

Table 4- Summary of the characterized components in the straw from foliar treatment in the greenhouse expressed as % TRR.

Component	Extractable			Bound		Total
	Organic	Aqueous	Aqueous + Cellulase	Organic	Aqueous	
Difenoconazole	43.3	1.2	0.8	0.1	-	45.4
CGA-205374	0.5	-	0.5	<0.1	0.6	1.6
CGA-205375	2.2	0.3	13.4	0.4	1.0	17.3
Triazole	3.4	-	-	0.1	1.7	5.2
Triazole Alanine	-	-	-	-	1.4	1.4
Triazole Acetic Acid	-	-	-	-	1.1	1.1
Total	49.4	1.5	14.7	0.6	5.8	72.0

Side-By-Side Comparison of Seed- and Foliar-Treated Straw Residues: Samples of foliar- and seed-treated extracts were fractionated as described above. The portion of the residue partitioning into the organic phase was greater in the foliar-treated than seed-treated samples (Table 2), indicating a greater extent of difenoconazole metabolism in the seed-treated plants. The organic extracts were compared using 1D-TLC (Table 5). *Difenoconazole per se* was the major component in the foliar-treated plants while CGA-205375 was the major component identified in the seed-treated samples.

Table 5- Comparison of organic-soluble components in straw extracts by 1-D TLC from seed- and foliar-treatment.

Component	Seed-Treated (Field)		Seed-Treated (Greenhouse)		Foliar-Treated (Greenhouse)	
	ppm	% TRR	ppm	% TRR	ppm	% TRR
A1	0.0007	1.23	0.0035	4.35	3.62	6.73
A2	0.0001	0.20	0.0012	1.53	0.66	1.22
CGA-205375	0.0016	2.58	0.0040	4.97	2.22	4.12
A4	-	-	0.0003	0.36	0.27	0.51
CGA-205374	-	-	0.0005	0.62	0.61	1.13
Difenoconazole	0.0002	0.39	0.0003	0.31	21.25	39.50
A7	0.0001	0.13	0.0002	0.20	0.46	0.86
A8	0.0021	3.41	0.0001	0.12	0.11	0.21
A9	-	-	0.0003	0.35	0.05	0.09
A10	-	-	-	-	0.02	0.03
A11	0.0001	0.16	0.0001	0.13	-	-

The aqueous-soluble residues were also compared by 1D-TLC (Table 6). A large portion of the TRR was identified as triazole alanine and triazole acetic acid in the seed-treated samples. Unlike the foliar-treated-samples, cellulase incubation released very little (2.5-3.5% of the TRR) organic-soluble material. Incubation of the seed-treated bound residues with protease reduced the amount of unextractable residues to 8.1% (field-grown) and 9.7% of the TRR (greenhouse-grown). The released residues were fractionated and derivatized as described above. The initial TLC profiles of the seed- and foliar-treated residues were similar, but further identification was not performed. The total of identified residues in the seed-treated samples was 65.2% of the TRR in field-grown wheat straw (Table 7) and was 42.2% of the TRR in those grown in the field (Table 8). The major metabolites identified were triazole alanine and triazole acetic acid.

Table 6- Comparison of aqueous-soluble components in straw extracts by 1-D TLC from seed- and foliar-treatment.

Component	Seed-Treated (Field)		Seed-Treated (Greenhouse)		Foliar-Treated (Greenhouse)	
	ppm	% TRR	ppm	% TRR	ppm	% TRR
A1	0.0004	0.58	0.0037	4.57	0.29	0.54
A2	0.0003	0.53	0.0020	2.49	0.18	0.33
A3	0.0078	12.77	0.0019	2.42	0.31	0.57
Triazole Alanine	0.0226	36.97	0.0096	11.82	0.49	0.91
A5	0.0040	6.60	0.0029	3.53	0.54	1.01
Triazole Acetic Acid	0.0154	25.22	0.0193	23.81	0.31	0.57
A7	-	0.05	0.0006	0.76	0.28	0.52
A8	-	-	0.0005	0.66	0.72	1.35
A9	-	-	0.0012	1.5	3.41	6.34
A10	0.0006	1.04	0.0006	0.76	1.03	1.92
A11	-	-	0.0009	1.17	0.46	0.86
A12	0.0007	1.20	0.0007	0.82	0.37	0.68
A13	0.0004	0.59	0.0005	0.59	1.35	2.51
A14	-	-	0.0005	0.64	0.43	0.80
CGA-205375	-	-	0.0002	0.26	0.83	1.54
A16	-	-	0.0005	0.60	0.52	0.97
CGA-205374	-	-	0.0004	0.44	0.81	1.51
A18	0.007	1.14	0.0005	0.64	0.04	0.07

Table 7- Summary of the characterized components in the seed-treated, field-grown straw samples.

Component	Organic-soluble		Aqueous-Soluble		Total	
	ppm	% TRR	ppm	% TRR	ppm	% TRR
Difenoconazole	0.0002	0.39	-	-	0.0002	0.39
CGA-205374	-	-	-	-	-	-
CGA-205375	0.0016	2.58	-	-	0.0016	2.58
Triazole Alanine	-	-	0.0226	36.97	0.0226	36.97
Triazole Acetic Acid	-	-	0.0154	25.22	0.0154	25.22
Total	0.0018	2.97	0.0380	62.19	0.0398	**65.16**

Table 8- Summary of the characterized components in the seed-treated, greenhouse-grown straw samples.

Component	Organic-soluble		Aqueous-Soluble		Total	
	ppm	% TRR	ppm	% TRR	ppm	% TRR
Difenoconazole	0.0003	0.31	-	-	0.0003	0.31
CGA-205374	0.0005	0.62	0.0004	0.44	0.0009	1.06
CGA-205375	0.0040	4.97	0.0002	0.26	0.0042	5.23
Triazole Alanine	-	-	0.0096	11.82	0.0096	11.82
Triazole Acetic Acid	-	-	0.0193	23.81	0.0193	23.81
Total	0.0048	5.90	0.0349	36.33	0.0343	**42.23**

CBTS' Conclusion: As requested in our previous review, the registrant has performed further metabolite identification work on the labelled wheat samples. As these samples were 3.5 years old at the time of this study, storage stability is an important consideration. The registrant has shown that the fractionation behavior of the samples to be basically unchanged during storage. However, no chromatographic evidence of storage stability was submitted. CBTS is unable to asses the stability of these samples without examining the chromatographic data. The registrant should submit chromatograms of the triazole-labelled grain and straw samples before and after storage so that we can be assured of stability during storage.

The TRR in the seed-treated grain samples was significantly larger when analyzed for this study than was determined previously (Table 2). The registrant suggests that desiccation of the sample could account for the difference and proposes that the original value be used to estimate the magnitude of the individual components of the residue. However, the increase in TRR of this sample (3.2X) is too large to be accounted for by desiccation and may be a result of incomplete homogenization of the sample. CBTS will use the new (greater) value as a worst case estimate. The registrant extracted the grain samples and fractionated the soluble residue into two peaks on a sephadex column. The major peak was separated into four zones using preparative TLC. One of these zones was identified as triazole (13% of the TRR of the seed-treated sample). Further work was performed only on the foliar-treated grain samples (Table 3). The residues identified were triazole (49.3% of the TRR) and triazole acetic acid (16.0% of the TRR). However, several fractions from the TLC separation contained >0.05 ppm and/or >10% of the TRR but were not further characterized. CBTS concludes that the identification of the residues in the seed-treated grain samples is not adequate. The registrant has demonstrated that the metabolism of difenoconazole in the seed- and foliar-treated plants appears to be similar. But without performing a complete metabolite identification on the seed-treated samples, we are unable to estimate the amount of the metabolites which would be present in the actual field samples. The registrant should perform the same procedures on the seed-treated grain samples as were performed on the foliar-treated samples and should also further characterize/identify any fraction (i.e., Zones A, B, D - Table 3) which contain >10% of the TRR or >0.05 ppm. The registrant must convince us that there is no single unidentified compound which exceeds these trigger values in the seed-treated grain sample.

Pending the demonstration of storage stability, CBTS considers the nature of the residue in wheat straw to be understood. The metabolites identified in the seed-treated straw were difenoconazole *per se* (0.3-0.4% of the TRR), CGA-205374 (0-1.1% of the TRR), CGA-205375 (2.6-5.2% of the TRR), triazole alanine (11.8-37.0% of the TRR) and triazole acetic acid (23.8-25.2% of the TRR). No other single compound appeared to exceed 0.05 ppm or 10% of the TRR.

The registrant has not reported any further attempts to characterize the nature of the residue in wheat forage. Wheat tops harvested 40 days after planting treated seeds contained significant amounts of both phenyl- (0.075 ppm) and triazole-labelled (0.148 ppm) residues (MRID# 420900-33). As the label allows grazing 55 days after planting, the nature of the residue should be determined in immature (40 day) wheat. The registrant should determine the nature of the residue in both the phenyl- and triazole-labelled tops harvested 40 days after planting. Evidence of storage stability of these samples should also be provided.

CBTS will refer to the Metabolism Committee on the toxicological significance of metabolites once the deficiencies associated with plant metabolism have been addressed. A decision by CBTS concerning which

residues to regulate will then follow. If a tolerance on the parent only is not appropriate, a revised Section F and additional field studies, analytical methodology, and storage stability data may be needed.

In summary, the registrant should provide: **1)** chromatographic evidence of storage stability of the labelled grain, straw and forage samples; **2)** further characterize the nature of the residue in the triazole-labelled seed-treated grain samples by performing the same procedures on the seed-treated grain samples as were performed on the foliar-treated samples and also further characterizing/identifying any fraction which contains >10% of the TRR or >0.05 ppm (i.e., Zones A, B and C from TLC separation). If there is insufficient radioactivity in these Zones for adequate identification/characterization, then the foliar-treated grain samples should be further characterized. The registrant must convince us that there is no single unidentified compound which exceeds these trigger values in the seed-treated grain sample; and **3)** characterize the nature of the residue in both the phenyl- and triazole-labelled whole plants harvested 40 days after planting.

NATURE OF THE RESIDUE- ANIMALS

Deficiency - Conclusion 3 (from Memo, R. Lascola 10/26/92)

CBTS concludes that the nature of the residue in animals is adequate for this imported crop from treated seed use. For any future tolerance request, the petitioner must address the following concerns: **a)** The petitioner has failed to take all reasonable steps to identify or release aqueous phase and conjugated metabolites which comprise up to half of the observed activity in several tissues. The petitioner has not noted the effects of acidic or basic hydrolysis on these metabolites, nor has mass spectrometry been used to identify the metabolites. **b)** While the metabolite CGA-205375 appears to be the major organic-soluble metabolite, inconsistencies between the triazole- and phenyl-labeled experiments bring the measured residue levels of this compound into question. *Specifically, bridge-intact metabolites* should appear in approximately the same proportion in the two studies, and they do not. CBTS asks the petitioner to resolve these inconsistencies. **c)** The petitioner should also explain the large radioactivity recoveries (>>120%) reported for several samples. If the petitioner has stored extra samples from these studies under frozen conditions, reanalysis of the tissues may be attempted, taking care to address the concerns listed above. In that event, the petitioner should also supply information detailing the stability of the chemical and metabolites under the storage conditions. Otherwise, the petitioner will have to reconduct these studies.

Petitioner's Response: [^{14}C]-CGA-169374 phenyl and triazole label distribution, elimination, and metabolism in hens. Amendment 1. (MRID# 431203-01)

CBTS' Conclusion: This amendment corrects an error in Table X of the original report (MRID# 420900-41) in which the ppm values of two metabolites in kidney were transposed. The conclusions on this study were based on the %ppm values which are not affected by this amendment.

The requested information has not been provided. **This deficiency remains outstanding.**

ANALYTICAL ENFORCEMENT METHODOLOGY- PLANTS

Existing analytical enforcement methodology ia adequate to support the requested difenoconazole tolerances on wheat and barley RACs (Memo, G. Kramer 1/10/94). The method is described in MRID# 428065-04 and has undergone successful PMV. The petitioner validated the method at 0.01 ppm in grain and 0.05 ppm in straw and forage. ACL validated the method at 0.055 ppm in all RACs (Memo, R. Lascola 12/28/92).

ANALYTICAL ENFORCEMENT METHODOLOGY- ANIMAL RACs

Submitted with this petition:

Difenoconazole (CGA-169374) Analytical Method for the Determination of CGA-169374 Residues in Dairy and Poultry Tissue, Eggs and Milk by Gas Chromatography. (MRID# 428180-04)

and

Method Validation Ruggedness Trial for the Determination of CGA-169374 in Beef Liver, Eggs, and Milk Using Analytical Method AG-544, "Analytical Method for the Determination of CGA-169374 Residues in Dairy and Poultry Tissue, Eggs and Milk by Gas Chromatography." (MRID# 428180-05)

Procedure: The sample is extracted by homogenization for 1 min with 95:5 acetonitrile:concentrated ammonium hydroxide. After filtration, the extract is diluted with water and saturated NaCl and partitioned with hexane. The hexane fraction is partitioned with acetonitrile and the acetonitrile fraction is cleaned-up on a silica gel SepPak. The final extract is analyzed by packed column GC using alkali flame ionization detection.

Results: RAC samples were fortified with difenoconazole and analyzed with the proposed analytical enforcement method. Four samples were prepared of each RAC- two at the proposed tolerance plus one each at 5X and 10X. Acceptable recoveries were obtained for each RAC at the level of the proposed tolerances (Table 9). The average recovery was 99 ± 12% (n=52).

ILV: The submitted ILV (MRID# 428180-05) appears to have been performed at the same lab (Residue Chemistry Dept., Ciba-Geigy, Greensboro) in which the method was developed. The registrant claims that this study is independent since the analysts involved had no prior experience with the method. The method was successfully validated in beef liver (0.05, 0.1 and 0.25 ppm), eggs (0.05, 0.1 and 0.25 ppm), and milk (0.01, 0.02 and 0.05 ppm). The average recoveries were 96 ± 25% for liver, 103 ± 7% for eggs and 118 ± 5% for milk. We have forwarded the analytical method and ILV to the ACL, Beltsville for the PMV. CBTS

will withhold its conclusion on the adequacy of method AG-544 as an analytical enforcement method for difenoconazole residues in meat, milk and eggs pending the outcome of the PMV.

Table 9- Summary of recovery data for cattle and poultry RACs fortified with difenoconazole and analyzed with the proposed enforcement method.

RAC	% Recovery at Fortification (ppm) of:			
	0.01	0.05	0.10	0.5
Dairy Cattle				
Milk	134, 102	118	-	111
Round	-	110, 110	99	96
Loin	-	108, 108	104	99
Perirenal Fat	-	95, 108	97	95
Omental Fat	-	81, 81	98	94
Kidney	-	89, 89	96	102
Liver	-	121, 121	109	109
Blood	-	110, 98	99	93
Poultry				
Lean Meat	-	76, 91	91	86
Liver	-	97, 97	92	91
Fat	-	103, 103	98	110
Skin	-	92, 98	95	100
Eggs	-	74, 81	81	83

STORAGE STABILITY

Deficiency - Conclusion 7 (from Memo, R. Lascola 10/26/92)

Should the petitioner wish to pursue a domestic registration for use of CGA-169374 on any wheat, barley, or rye commodity in the future, storage stability data on a cereal grain crop (including grain, forage, and fodder) will have to be provided. Also in that case, any conclusions concerning the adequacy of the storage stability data would be withheld until the nature of the residue in cereal grains has been determined.

Petitioner's Response: MRID# 428180-03. Samples of lettuce, soybeans and wheat forage were fortified with difenoconazole at a level of 0.20,

0.20 and 0.50 ppm, respectively, and stored at -20 °C for 1 yr. The stored samples were prepared in duplicate. The samples were analyzed by method AG-514 which was reviewed by CBTS in conjunction with other storage stability studies in potatoes and tomatoes (Memo, R. Lascola 10/26/92). The results are shown in Table 10.

Table 10- % Recovery of difenoconazole from fortified RACs after storage at -20 °C.

RAC	Fortification Level (ppm)	Storage Interval (months)	Fresh Fortification Recovery	Apparent Recovery in Stored Sample	Corrected Recovery in Stored Sample
Lettuce	0.20	0	-	75	-
		1	100	100	100
		3	115	110	96
		6	95	98	103
		12	105	118	112
Soybean	0.20	0	-	88	-
		1	130	120	92
		3	125	110	88
		6	125	92	74
		12	110	125	114
Wheat Forage	0.50	0	-	93	-
		1	98	120	122
		3	112	110	98
		6	102	88	86
		12	118	93	79

CBTS' Conclusion: This study demonstrates adequate storage stability in lettuce, soybeans, and wheat forage for a period of 1 yr. However, storage stability studies are required for all plant parts for which tolerances are required; i.e., for wheat and barley: forage, grain, hay and straw. For this petition, the registrant should perform storage stability studies on at least the RACs wheat (or barley) grain, and straw. Since the samples in the magnitude of the residue trials were stored for up to 12 months, the storage interval in this study should be at least 1 yr.

MAGNITUDE OF THE RESIDUE- PLANTS

Two magnitude of the residue studies were reviewed in conjunction with PP#2E4051 (Memo, R. Lascola 10/26/92). One of these studies was conducted in Europe and will thus will not be considered in conjunction with this petition for domestic tolerances. In the U.S. study, the following trials were conducted in which residues in forage, grain and straw RACs were determined: 4 winter trials in 4 different states (representing 38% of the U.S. winter wheat acreage in 1991, *Agricultural Statistics 1992*) and 7 spring trials in 7 different states (representing 97% of the U.S. spring wheat acreage in 1991, *Agricultural Statistics 1992*). Two additional winter wheat trials were conducted, but the results can not be considered to be reliable since forage samples were not taken due to poor growth. The treatment rate was 1X and 2X of the maximum label application rate. Detectable residues were found in one spring wheat forage sample (0.01 ppm, 1X rate), two winter wheat forage samples (0.02 ppm, 1X and 2X), two winter wheat grain samples (0.01 ppm, 1X and 2X), and one winter wheat straw sample (0.03 ppm, 1X rate). No barley field trials were conducted in the U.S. **CBTS concludes that this data is not adequate to support this request for domestic tolerances on wheat and barley RACs.** The number of field trials and geographic representation is insufficient for winter wheat. In addition, the registrant failed to generate data for wheat hay, which may be reinstated as a RAC in Table II. Wheat hay was in the original Table II, but then deleted as announced in the FIFRA '88 Phase 3 Technical Guidance Package. It may be reinstated in the forthcoming revision of Table II. Also, data from barley field trials in the U.S. should be submitted to support tolerances on this crop. The registrant is requested to perform at least 4 barley field trials (in ND, MT, MN plus one other state such as ID, SD or WA) and at least 8 additional wheat field trials (in KS, OK, CO, NE and WA plus three other states such as MO, SD, MT, OH, IL or IN). Residue data for grain, straw and forage should be obtained in these trials. **Data for and a revised Section F with proposed difenoconazole tolerances on wheat and barley hay may also be required in the future.**

If additional metabolites are determined to be of concern, the petitioner will either have to conduct new field trials to detect those compounds, or reanalyze any stored samples available from the above trials. If the latter option is chosen, appropriate storage stability data will have to be provided.

MAGNITUDE OF THE RESIDUE- PROCESSED FRACTIONS

CBTS has previously reviewed a processing study for spring wheat which was seed-treated (2X) and also foliar-treated (10X) 28 days before harvest (Memo, R. Lascola 10/26/92). No residues (<0.01 ppm) were detected in grain or any processed fraction. Food additive tolerances are thus not needed for difenoconazole *per se*. If the Metabolism

Committee determines any other metabolites to be of regulatory concern, then processing studies will be needed for these metabolites.

MAGNITUDE OF THE RESIDUE- ANIMALS

The registrant has requested (MRID# 428180-06) a waiver for animal feeding studies based on the low potential for residues in feed items and the exaggerated rates used in the animal feeding studies. Based on a diet comprised of 100% wheat RACs and residues at the level of the proposed tolerances, the maximum dietary burden for dairy cattle is estimated to be 0.30 ppm (Table 11). Two metabolism studies were performed in ruminants (lactating goats)- a 10 day study with a dose rate of 4.17 ppm (14X the 0.30 ppm estimated dietary burden) and a 3 day study with a dose rate of 100 ppm (333X the 0.30 ppm estimated dietary burden). The TRR in the goat tissues can be used to estimate the expected residues in a feeding study with a dose rate of 0.30 ppm (Table 12). The maximum residue observed was in liver, estimated to be at a level of 0.02 ppm from both metabolism studies. This value is 2.5X below the LOQ of the proposed analytical enforcement method (0.05 ppm). The estimated residue in milk would be 0.5 ppb, 20X below the method LOQ of 0.1 ppm.

Table 11- Estimated dietary burden of difenoconazole for dairy cattle using the maximum residues observed in wheat field trials.

RAC	% Diet	% DM	Proposed Tolerances (ppm)	Contribution to Diet
Forage	65	25	0.1	0.26
Straw	10	88	0.1	0.01
Grain	25	89	0.1	0.03
Total				**0.30**

Table 12- Estimated residues in dairy cattle RACs based on TRR of phenyl-labelled samples from metabolism studies and the estimated maximum dietary burden of difenoconazole from Table 11.

RAC	Residue at 4.17 ppm	Extrapolated Residue at 0.30 ppm	Residue at 100 ppm	Extrapolated Residue at 0.30 ppm
Milk	0.008	0.0005	0.163	0.0005
Kidney	0.064	0.005	1.748	0.005
Liver	0.259	0.019	6.658	0.020
Fat	0.025	0.002	0.618	0.002
Muscle	0.008	0.0005	0.207	0.0006

Grain is the only wheat RAC used as a feed item for laying hens. Based on the maximum percent in the diet (82%) and the proposed tolerance in grain (0.1 ppm), the dietary burden for hens is estimated to be 0.082 ppm. Two metabolism studies were performed in poultry (laying hens)- a 14 day study with a dose rate of 5.73 ppm (70X the 0.082 ppm estimated dietary burden) and a 3 day study with a dose rate of 68 ppm (829X the 0.082 ppm estimated dietary burden). The TRR in the hen tissues can be used to estimate the expected residues in a feeding study with a dose rate of 0.082 ppm (Table 13). The maximum residue observed was in egg yolk, estimated to be at a level of 0.01 ppm from the 14 day metabolism study. Egg yolk residues in the 3 day study were much lower due to insufficient time for transfer of residues to the yolks. This value is 5X below the LOQ of the proposed analytical enforcement method (0.05 ppm).

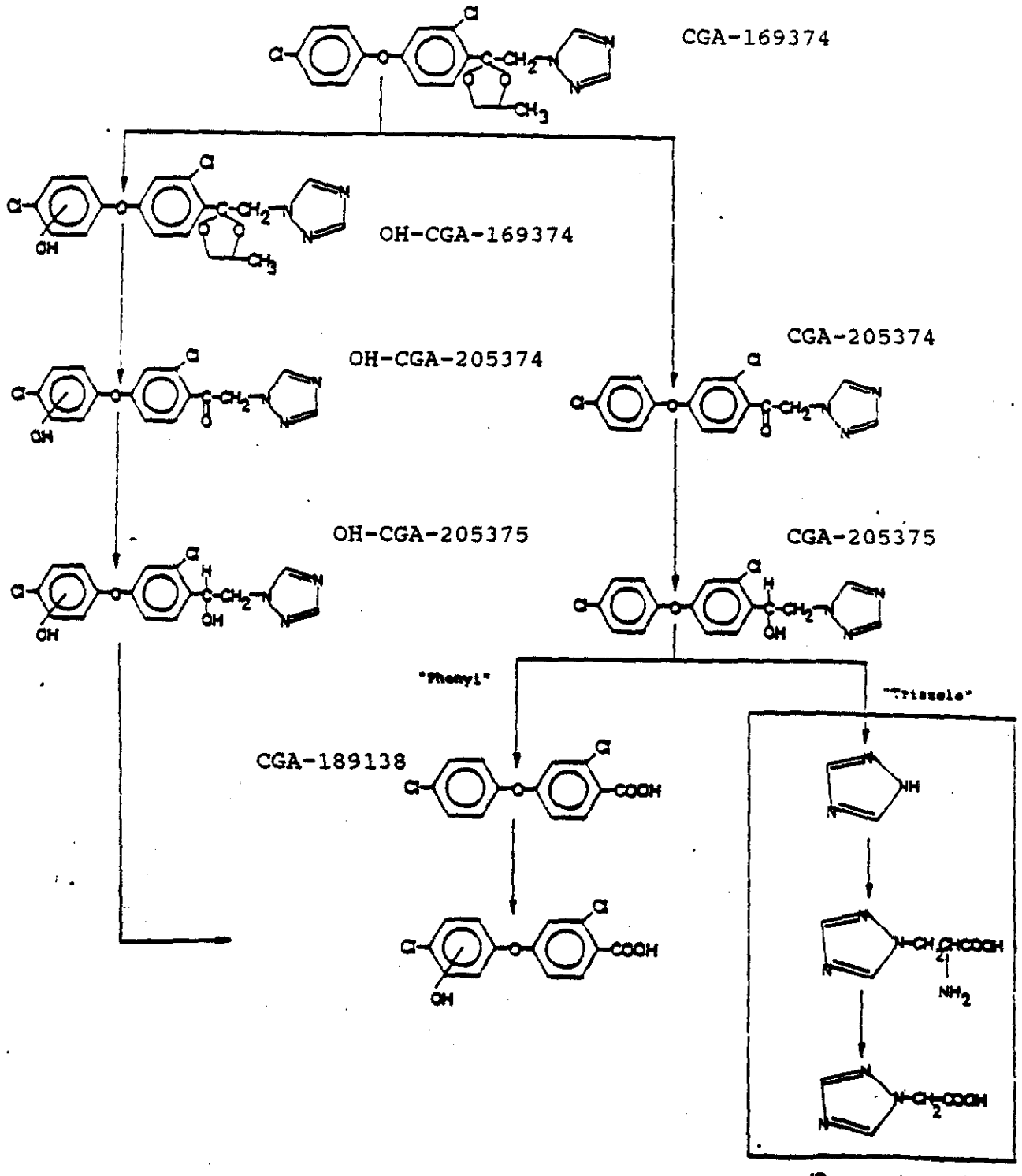
Table 13- Estimated residues in laying hen RACs based on TRR of phenyl-labelled samples from metabolism studies and the estimated maximum dietary burden of difenoconazole of 0.082 ppm.

RAC	Residue at 5.73 ppm	Extrapolated Residue at 0.082 ppm	Residue at 68 ppm	Extrapolated Residue at 0.082 ppm
Egg White	0.066	0.001	0.413	<0.001
Egg Yolk	0.718	0.01	0.272	<0.001
Skin/Fat	0.046	0.001	0.464	0.001
Liver	0.147	0.002	4.259	0.005
Kidney	0.522	0.007	1.886	0.002
Muscle	0.093	0.001	0.509	0.001

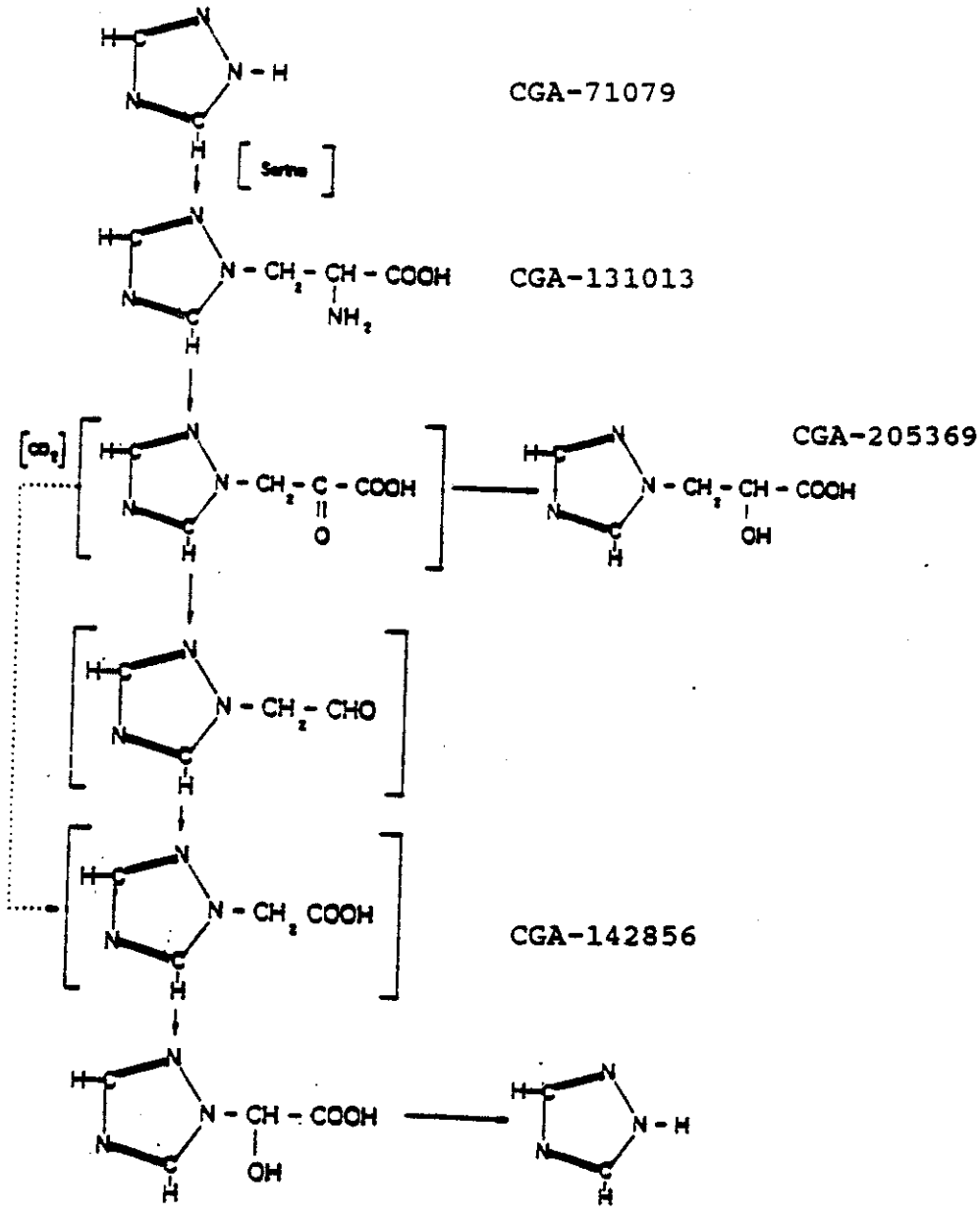
For now, CBTS is willing to accept the registrants proposal to allow the animal feeding studies to also serve as feeding studies. If higher levels of difenoconazole residues than previously observed are found in the new wheat or barley field trials or if the Metabolism Committee determines that metabolites other than difenoconazole *per se* to be of regulatory concern, then CBTS will recalculate the estimated exposere and may require the registrant to perform conventional feeding studies. Feeding studies in cattle and poultry, as appropriate, will be needed for any future tolerance requested on potential livestock feed commodities which could lead to higher residues of concern in meat, milk and eggs.

cc: PP#2F4107, Kramer, circ., R.F.
RDI: P.V. Errico (3/24/94), R.A. Loranger (3/25/94)
G.F. Kramer:804V:CM#2:(703)305-5079:7509C
USER\CB:difenoco.005

Plant Metabolite Structures and Pathways 1



(From MRID# 420900-33. CIBA-GEIGY Report No. ABR-90010)



(From MRID# 420900-33. CIBA-GEIGY Report No. ABR-90010)

F. Kres 1/25/94

Attachment:

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL difenoconazole*

CODEX NO. _____

CODEX STATUS:

[✓] No Codex Proposal Step 6 or Above

Residue (if Step 8): _____

PROPOSED U.S. TOLERANCES:

Petition No. 2F04107

CBTS Reviewer G.F. Kramer

Residue: parent only

Crop(s)	Limit (mg/KG)

Crop(s)	Limit (mg/KG)
Wheat Forage	-- 0.1 ppm
Barley Forage	-- 0.1 ppm
Wheat Straw	-- 0.1 ppm
Barley Straw	-- 0.1 ppm

CANADIAN LIMITS:

[✓] No Canadian Limits

Residue: _____

Crop(s)	Limit (mg/KG)

MEXICAN LIMITS:

[✓] No Mexican Limits

Residue: _____

Crop(s)	Limit (mg/KG)

NOTES

*1-{2-[4-(4-chlorophenoxy)-2-chlorophenyl]-4-methyl-1,3-dioxolan-2-yl-methyl}-1*H*-1,2,4-triazole

Attachment: Page 2 of 2

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL difenoconazole*

CODEX NO. _____

CODEX STATUS:

[✓] No Codex Proposal Step 6 or Above

Residue (if Step 8): _____

PROPOSED U.S. TOLERANCES:

Petition No. 2F04107

CBTS Reviewer G.F. Kramer

Residue: parent only

Crop(s)	Limit (mg/KG)
Milk --	0.01 ppm
Eggs --	0.05 ppm
Fat* --	0.05 ppm
Poultry Fat --	0.05 ppm
Meat* --	0.05 ppm
Poultry Meat --	0.05 ppm
Meat By-Products* --	0.05 ppm
Poultry Meat B-P --	0.05 ppm

*of cattle, goats, horses, hogs and sheep

CANADIAN LIMITS:

[✓] No Canadian Limits

Residue: _____

MEXICAN LIMITS:

[✓] No Mexican Limits

Residue: _____

Crop(s)	Limit (mg/KG)

Crop(s)	Limit (mg/KG)

NOTES

*1-{2-[4-(4-chlorophenoxy)-2-chlorophenyl]-4-methyl-1,3-dioxolan-2-yl-methyl}-1*H*-1,2,4-triazole

End of Document